NASA microgravity research highlights

The Bare Bones of Bioactive Glass

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In a laboratory in Philadelphia, Pennsylvania, a bone biochemist, a fluid mechanics specialist, and a biomaterials scientist are building the skeletal framework, so to speak, for advances in orthopedic and periodontal surgery. Paul Ducheyne, a principal investigator in the microgravity materials science program and head of the University of Pennsylvania's Center for Bioactive Materials and Tissue Engineering, is leading the trio as they use simulated microgravity to determine the optimal characteristics of tiny glass particles for growing bone tissue. The result could make possible a much broader range of synthetic bone-grafting applications.

Bone grafting is a procedure used to rebuild or strengthen bones that have been compromised through birth defects, injury (such as a break), or disease (such as osteoporosis). In many cases a physician uses autogenous bone (harvested from another site in the patient) or allograft bone (from a donor) to build a lattice that fills the void in the bone. Then the patient's own bone undergoes osteoinductive healing, in which osteoblasts, or bone-forming cells, replace the lattice as it is broken down and assimilated by osteoclasts, or bone-absorbing cells. The result is a bone with standard appearance, density, and function.

But harvesting the patient's own bone can add significant pain to a medical procedure, and donor bone may spark a latent fear of disease transmission (despite thorough treatment of the donor bone to remove all pathogens). When a patient prefers not to use human bone, physicians need a substitute. With the advent of ever-better synthetic materials, there is a greater tendency to move toward artificial bone graft materials.

Particles made of either polymers or glass can be used to aid in bone grafting in two ways. Inert polymer beads, with no special biological trigger, can serve as a permanent "scaffold" for supporting bone cells, when that is sufficient for the healing process. When more is needed to advance healing, bioactive glass beads, with ingredients similar to the two main components of the mineral in bone (calcium and phosphate), can be used to actually enhance bone growth.

The Backbone of the Research

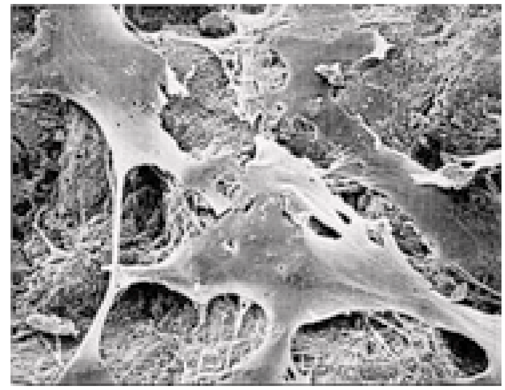
The bioactive glass beads, which can stimulate capillaries, perivascular tissues, and bone cells from the host to grow into the graft, were developed by Ducheyne before he began his collaboration with NASA. The beads have been available for bone grafting in periodontal work since the early 1990s. The material he uses in his NASA studies is made by immersing tiny bioactive glass beads in a solution containing serum proteins and calcium phosphate. By the time the beads have spent three weeks in the solution, the surfaces of the granules have transformed into a composite of porous carbonated calcium phosphate and proteins.

Ducheyne explains the significance of the surface transformation: "Bone is composed of two main components: organic material (mostly collagen) and a mineral face, an apatite containing primarily calcium phosphate, some carbonate, and hydroxyl ions. So we create an apatitic structure, making sure the properties of these microcarriers - including their morphology, pore size, and porosity - are as close as possible to those of the bone matrix."

The result is a material that is already widely accepted. "Dental application [of the granules] is very well established now," says Ducheyne. The material has been used on a few hundred thousand people for such procedures as rebuilding extraction sites or defects of the alveolar ridge, the part of the jaw where the teeth arise. He contrasts, "The orthopedics application has come somewhat more slowly, the reason being that this is a field where the surgical procedures by themselves are much more involved. Also, the physicians are more conservative, and rightfully so, because the consequences are much more serious if anything goes wrong. As a result, there are many more tests for us to make and more experiments left to conduct."

Boning Up on Beads in Microgravity

Ducheyne's team is conducting some of those needed experiments using a rotating wall bioreactor. The vessel is filled with fluid that rotates on its horizontal axis, causing its contents to be suspended, creating an environment with characteristics similar to those found in microgravity. These conditions provide a setting in which cells do not settle to the lower surface of the vessel, as they would in normal gravity in a petri dish. Instead, they can form three-dimensional arrays as they might in the human body. Ducheyne explains, "The carriers [beads] float in the circulating medium [in the bioreactor], and tissue forms on and around each of the carriers. Eventually this tissue bridges the individual carriers, and a three-dimensional structure is achieved."

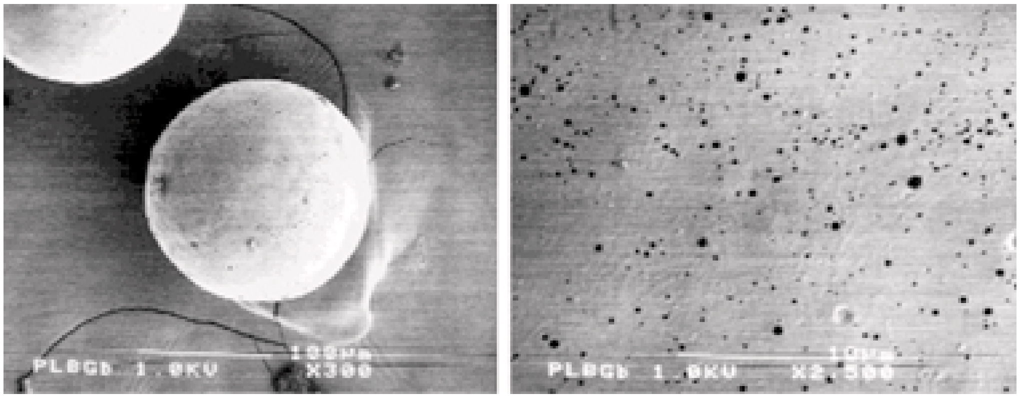


Even in normal gravity, bioactive glass particles enhance bone growth in laboratory tests with flat tissue cultures (above). Ducheyne and his team believe that using the bioactive microcarriers in a rotating bioreactor in microgravity will produce improved, three-dimensional tissue cultures.

Getting optimal results with the bioreactor requires attaining a delicate balance between the viscosity and composition of the fluid, the density of the particles, and the speed of rotation. This calls for the combined expertise of Ducheyne and his two colleagues. Ducheyne explains that getting the fluid composition and viscosity just right in the bioreactor is very important. "That's where the fluid mechanics specialist [Co-Investigator Portonovo Ayyaswamy, who is also the principal investigator for a NASA-funded companion research project] comes in," he says. "Inside the vessel, we add microcarriers [glass particles] with properties that cause bone cells to behave normally as they would in the body, and that's where the materials issues come in." Observing how the bone cells and the microcarriers interact is the job of the biochemist, Co-Investigator Irving Shapiro.

But even when the three specialists achieve the delicate balance they need on Earth, tissue cultures in the experiment hardware can only grow so large before gravity's pull causes the culture to sink. Taking the team's research to the International Space Station (ISS) would allow the culture to grow larger because the effects of gravity are minimized in a microgravity environment.

"Our ultimate goal," Ducheyne projects, "is to use bioactive glass particles as microcarrier beads for producing larger three-dimensional bone-tissue cultures in micro-



Bioactive glass particles (left) with a microporous surface (right) are widely accepted as a synthetic material for periodontal procedures. Using the particles to grow three-dimensional tissue cultures may one day result in developing an improved, more rugged bone tissue that may be used to correct skeletal disorders and bone defects.

gravity. This goal combines two potential methods of correction for bone defects and skeletal disorders. On the one hand, scientists have found that the environment of the rotating wall bioreactor enables three-dimensional tissue cultures to be successfully grown on inert microcarrier beads. On the other hand, in normal gravity, enhanced bone growth has occurred when bioactive glass particles have been present. Bringing together these two concepts is a logical next step. Since the glass particles actually promote bone growth rather than just serve as a template (as inert microcarriers do), their use will lead to improved tissue cultures."

At this point, Ducheyne is studying possible effects of microgravity on the transformation of the microcarriers to a bioactive material. He explains, "The conditions in orbit and also the conditions in a rotating wall vessel are different from normal cell culture conditions. So that then means that the reactions at the surface of these microcarriers can be totally different from what we know. And so we need to figure out what these reactions are, both the kind of reactions and the kinetics of those reactions." After Ducheyne makes those determinations, he and his team would like to take their experiment to the ISS for growing tissue samples.

"Taking the research to the ISS is so important because conditions in the rotating wall vessel [in orbit] will allow us to get more extensive amounts of tissue with uniform properties created outside of the body than we could on the ground. Once we've gone as far as we can on Earth and gleaned as much information as possible, then we have to validate results by conducting the experiment also in space."

Finding the Wishbone

The synergy of combining the expertise of the scientists in the trio is leading them along a path toward improving human life. Funded by grants from both NASA's microgravity materials science and biotechnology programs, their research may provide keys to understanding how to produce large tissues for medical applications. "We look at both sides of the equation, both the materials as well as the biological aspect, and of course, we're excited about using whatever we learn for the benefit of patient health and well-being," summarizes Ducheyne.

As the scientists at the Center for Bioactive Materials and Tissue Engineering progress in their findings, they hope that their results will be put to good use in clinical trials here on Earth. Synthetic bone grafting might eventually be used for such procedures as vertebral fracture augmentations, used to treat spinal injuries where the vertebrae have become compressed due to fractures caused by osteoporosis. The material also might be used for spinal fusion, spinal revision and reconstruction, and even total joint implants. Development of an improved, more rugged bone tissue that may be used for implantation could provide therapy to correct skeletal disorders, bone defects, and other diseases of the bone. The research may also aid in developing the capability to grow bones in required shapes to replace or supplant bone that is missing because of birth defects or trauma.

In addition, an understanding of the fundamental changes that occur to bone tissue under conditions found in the rotating wall bioreactor could yield important information that will help in preventing or minimizing astronaut bone loss, a concern associated with long-term space travel. Ducheyne explains that this has always been a goal of the research: "I was aware of the peril of space travel related to the sometimes weakened skeletal structure of astronauts. And I had quite an extensive program here developing materials for strengthening and repairing bone when I heard about the research announcement. One of my colleagues said, 'Paul, we can make a difference.' I listened to him, and we took it from there and really got very excited about it."

Using the bioactive granule technology to maximize the strength of astronauts' bones after a flight would help maximize their quality of life on the ground or back in space. And it only seems fair that an experiment that likely will benefit from being conducted in space be capable of benefiting the health of the astronauts who will serve as its caretakers.

Additional information

OBPR: *http://spaceresearch.nasa.gov*
Microgravity research: *http://microgravity.nasa.gov*
Microgravity newsletter: *http://mgnews.msfc.nasa.gov*

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